

WHAT IS CLAIMED IS:

1. A method of treating a mammal having a disorder of cholesterol metabolism comprising administering to said mammal a therapeutically effective
5 amount of a compound that modulates the biological activity of ABCA1 polypeptide.

2. The method of claim 1, wherein said biological activity is *in vitro* lipid transport across a membrane.

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3. The method of claim 2, wherein said lipid is a member selected from the group consisting of phospholipid and cholesterol.

4. The method of claim 2, wherein said ABCA1 polypeptide comprises the
15 amino acid sequence of SEQ ID NO: 1.

5. The method of claim 2, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

20 6. The method of claim 1, wherein said biological activity is *in vitro* ion transport across a membrane.

7. The method of claim 6, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

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8. The method of claim 6, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

9. The method of claim 1, wherein said biological activity is *in vitro*
30 interleukin-1 transport across a membrane.

10. The method of claim 9, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

11. The method of claim 9, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

12. The method of claim 1, wherein said biological activity is *in vitro* ATP-hydrolysis.

13. The method of claim 12, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

14. The method of claim 12, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

15. The method of claim 1, wherein said biological activity is *in vitro* ATP-binding.

16. The method of claim 15, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

17. The method of claim 15, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

18. The method of claim 1 wherein said mammal is a mouse.

19. The method of claim 1 wherein said mammal is a human.

20. The method of claim 1, wherein said mammal has low HDL cholesterol levels relative to normal.

21. The method of claim 20 wherein said mammal is a mouse.

22. The method of claim 20 wherein said mammal is a human.

5 23. The method of claim 1 wherein said modulation is an increase in biological activity.

24. A method of treating a mammal having or at risk of developing a cardiovascular disease, comprising administering to said mammal a
10 therapeutically effective amount of a compound that modulates the biological activity of ABCA1 polypeptide.

25. The method of claim 24, wherein said biological activity is *in vitro* lipid transport across a membrane.

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26. The method of claim 25, wherein said lipid is a member selected from the group consisting of phospholipid and cholesterol.

27. The method of claim 25, wherein said ABCA1 polypeptide comprises
20 the amino acid sequence of SEQ ID NO: 1.

28. The method of claim 25, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

25 29. The method of claim 24, wherein said biological activity is *in vitro* ion transport across a membrane.

30 30. The method of claim 29, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

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31. The method of claim 29, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

32. The method of claim 24, wherein said biological activity is *in vitro* interleukin-1 transport across a membrane.

33. The method of claim 32, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

34. The method of claim 32, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

35. The method of claim 24, wherein said biological activity is *in vitro* ATP-hydrolysis.

36. The method of claim 35, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

37. The method of claim 35, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

38. The method of claim 24, wherein said biological activity is *in vitro* ATP-binding.

39. The method of claim 38, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

40. The method of claim 38, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

41. The method of claim 24 wherein said mammal is a mouse.

42. The method of claim 24 wherein said mammal is a human.

43. The method of claim 24, wherein said mammal has low HDL cholesterol levels relative to normal.

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44. The method of claim 43 wherein said mammal is a mouse.

45. The method of claim 43 wherein said mammal is a human.

10 46. The method of claim 1 wherein said disease is selected from the group consisting of Alzheimer's disease, Niemann-Pick disease, Huntington's disease, x-linked adrenoleukodystrophy, and cancer.

47. The method of claim 46 wherein said mammal is a mouse.

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48. The method of claim 46 wherein said mammal is a human.

49. The method of claim 24, wherein said cardiovascular disease is coronary artery disease, cerebrovascular disease, coronary restenosis, or
20 peripheral vascular disease.

50. A method of preventing cardiovascular disease in a human, said method comprising administering to said human an expression vector comprising an *ABCA1* polynucleotide operably linked to a promoter, said *ABCA1*
25 polynucleotide encoding an *ABCA1* polypeptide having *in vitro* *ABCA1* biological activity.

51. A method of preventing or ameliorating the effects of a disease-causing mutation in an *ABCA1* gene in a human, said method comprising
30 introducing into said human an expression vector comprising a promoter

operably linked to an *ABCA1* polynucleotide encoding an *ABCA1* polypeptide having *in vitro* *ABCA1* biological activity.

52. A method of treating or preventing cardiovascular disease in an
5 animal, said method comprising administering to said animal a compound that mimics the activity of wild-type *ABCA1*.

53. The method of claim 52, wherein said animal is a human.

10 54. The method of claim 52 wherein said compound is a member selected from a group consisting of protein kinase A, protein kinase C, vanadate, okadaic acid, IBMX1, fibrates, γ -estradiol, arachidonic acid derivatives, WY-14,643, LTB₄, 8(s)HETE, thiozolidinedione antidiabetic drugs, 9-HODE, 13-HODE, nicotinic acid, HMG CoA reductase inhibitors, and compounds that increase PPAR-
15 mediated *ABCA1* expression.

55. The method of claim 52, wherein said cardiovascular disease is coronary artery disease, cerebrovascular disease, coronary restenosis, or peripheral vascular disease.

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56. The method of claim 53 wherein said compound is a member selected from a group consisting of protein kinase A, protein kinase C, vanadate, okadaic acid, IBMX1, fibrates, γ -estradiol, arachidonic acid derivatives, WY-14,643, LTB₄, 8(s)HETE, thiozolidinedione antidiabetic drugs, 9-HODE, 13-HODE, nicotinic
25 acid, HMG CoA reductase inhibitors, and compounds that increase PPAR-mediated *ABCA1* expression.

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